

Please amend the second paragraph on page 16, lines 21-24, with the following paragraph:

AJ
Figure 2 represents the sequence of the NS1 protein of dengue virus serotype 1 (SEQ ID NO: 1), obtained with clone 4C of Example 2 below, and also the corresponding coding sequence (SEQ ID NO: 2).

Please replace the Sequence Listing originally filed with the application with the Sequence Listing submitted herewith.

IN THE CLAIMS:

Please cancel claims 1-20.

Please add the following new claims:

SUB B
21. (NEW) A method for the early detection of a flaviviral infection comprising:
detecting an NS1 nonstructural glycoprotein of a flavivirus in a biological sample by an immunological method using at least two antibodies,
wherein the biological sample is obtained at anytime throughout the duration of the clinical phase of the infection,
wherein the two antibodies may be identical or different,
wherein a first antibody, called a capture antibody, is either (1) a polyclonal antibody preselected by immunocapture on the NS1 protein of the flavivirus, wherein the NS1 protein is in hexameric form, or (2) a mixture of purified anti-NS1 monoclonal antibodies preselected for their high affinity for the NS1 protein of the flavivirus, wherein the NS1 protein is in hexameric form, and

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

wherein a second antibody, called a revelation antibody, is a polyclonal antibody directed against the NS1 protein in hexameric form or a mixture of monoclonal antibodies directed against an NS1 protein in hexameric form.

22. (NEW) The method as claimed in claim 21, wherein the flaviviral infection is an infection of the dengue virus.

23. (NEW) The method as claimed in claim 21, wherein the first antibody is attached to a solid support and the second antibody is optionally conjugated to a label.

24. (NEW) The method as claimed in claim 23, wherein if the second antibody is not conjugated to a label, binding of the second antibody to the NS1 protein attached to the solid support is detected with a third antibody conjugated to a label.

25. (NEW) The detection method as claimed in claim 24, wherein the label conjugated to the third antibody is an enzyme.

26. (NEW) The detection method as claimed in claim 25, wherein

(A) the first antibody is a mouse polyclonal antibody selected by immunocapture of the NS1 protein of the dengue virus, wherein the NS1 protein is in hexameric form, and

(B) the second antibody is a polyclonal antibody from a rabbit immunized with the NS1 protein of dengue virus serotype 1, wherein the NS1 protein is in hexameric form,

(C) the third antibody reveals binding of the second antibody to NS1 protein, and the third antibody is an antibody conjugated to peroxidase and directed against the second antibody.

27. (NEW) A boxed set for the early diagnosis of a flaviviral infection, comprising:

SUB
B/C

al

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

(A) a first antibody, called a capture antibody, which is either (1) a polyclonal antibody preselected by immunocapture on the NS1 protein of the flavivirus, wherein the NS1 protein is in hexameric form or (2) a mixture of purified anti-NS1 monoclonal antibodies preselected for their high affinity for the NS1 protein of the flavivirus, wherein the NS1 protein is in hexameric form;

(B) a second antibody, called a revelation antibody, is a polyclonal antibody directed against NS1 protein in hexameric form or a mixture of monoclonal antibodies directed against a NS1 protein in hexameric form;

(C) at least one positive control comprising an NS1 protein of a flavivirus, wherein the NS1 protein is in hexameric form; and,

(D) at least one negative control comprising a normal, uninfected human serum.

28. (NEW) The boxed set as claimed in claim 27, wherein the NS1 protein is obtained from a culture supernatant either from infected mammalian cells or from mammalian cells transfected with a recombinant plasmid comprising a gene for an NS1 protein of a flavivirus or a fragment of the gene or a fragment of the flaviviral genome, the fragments being capable of expressing all or part of the NS1 protein.

29. (NEW) The boxed set as claimed in claim 27 wherein the NS1 protein is from a dengue virus.

30. (NEW) The boxed set for the early diagnosis of a flaviviral infection as claimed in claim 28, wherein the recombinant plasmid was deposited with the Collection Nationale de Cultures et de Microorganismes under the number I-2220.

31. (NEW) A method for purifying an NS1 protein of a flavivirus, wherein the NS1 protein is in hexameric form, from a culture supernatant either of infected

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

mammalian cells or of mammalian cells transfected with a recombined plasmid, comprising:

- Sub
Bl cont'd
- (A) expressing the NS1 protein or a fragment of the NS1 protein from an NS1 gene or a fragment of the flaviviral genome, wherein the fragments are capable of expressing the NS1 protein prior to the purification of the NS1 protein;
 - (B) treating the NS1 protein with a precipitating agent;
 - (C) centrifuging the treated NS1 protein; and,
 - (D) separating a soluble form of the NS1 protein from a microparticulate form of NS1 protein.

32. (NEW) The method for purifying NS1 protein as claimed in claim 31, wherein the flavivirus is a dengue virus.

33. (NEW) The method for purifying NS1 protein as claimed in claim 32, wherein the flavivirus is dengue virus serotype 1.

34. (NEW) An immunogenic composition, comprising as the active principle, an NS1 protein of a flavivirus, wherein the NS1 protein is in hexameric form, optionally associated with other proteins, and at least one pharmaceutical vehicle.

35. (NEW) The immunogenic composition as claimed in claim 34, wherein the composition further comprises at least one mixture of NS1 proteins in hexameric form of a dengue virus serotype.

36. (NEW) A method for preparing an immunogenic composition capable of inducing the production of antibodies *in vivo* comprising combining an NS1 protein in hexameric form, or an NS1 protein expressed from a system for the expression of NS1 protein in hexameric form, with at least one pharmaceutical vehicle.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com